

PATENT SPECIFICATION

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(54) PROCESS FOR PREPARING MERCAPTOCARBOXYLIC ACID ESTERS

(71) We, SANKYO ORGANIC CHEMICALS COMPANY LIMITED, a Japanese body corporate, of 788, Kuji, Takatsu-ku, Kawasaki-shi, Kanagawa-ken, Japan, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to a process for preparing mercaptocarboxylic acid esters.

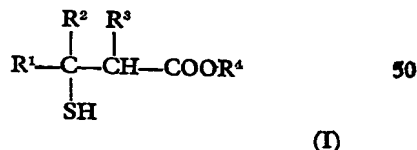
Mercaptocarboxylic acid esters are useful as starting materials in the preparation of various industrial chemicals and, in particular, they can be reacted with alkyltin compounds to produce highly efficient stabilizers for synthetic resins. They have previously been synthesized by adding a hydrogen halide to the double bond of an α,β -unsaturated carboxylic acid ester and reacting the resulting halocarboxylic acid ester with thiourea or an alkali metal hydrosulphide; but this is a lengthy process and unsatisfactory on an industrial scale. They are also formed as by-products in the reaction of α,β -unsaturated carboxylic acid esters with hydrogen sulphide; but this process is unsuitable for the production of mercaptocarboxylic acid esters, because large quantities of thiodicarboxylic acid esters are formed.

In our Specification Serial No. 1358019, we describe and claim a process by which β -mercaptopropionic acid and its esters can be prepared in high yield and in a simple manner, which comprises reacting acrylic acid or an ester thereof with ammonium hydrosulphide, an alkali metal hydrosulphide or an alkaline earth metal hydrosulphide in the presence of carbon disulphide, and acidifying the product of the reaction. It has now been discovered that this process can be extended to cover the preparation of other mercapto-

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carboxylic acid esters from the corresponding α,β -unsaturated carboxylic acid esters, with the same advantages of high yield and ease of operation. 45

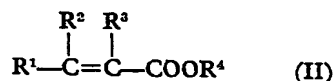
Accordingly, the invention provides a process for preparing a mercaptocarboxylic acid ester of formula:



wherein:

each of R^1 , R^2 and R^3 is a hydrogen atom, an alkyl group, an unsaturated hydrocarbon group, a carboxy-substituted alkyl group, a carboxy-substituted unsaturated hydrocarbon group, an alkoxycarbonyl-substituted alkyl group, an alkoxycarbonyl-substituted unsaturated hydrocarbon group, a phenyl group, a substituted phenyl group, a carboxyl group or an alkoxycarbonyl group, provided that R^1 , R^2 and R^3 may not all simultaneously be hydrogen atoms; and 55

R^4 is a phenyl or substituted phenyl group, or a residue derived by removal of a hydroxyl group from an alcohol; which comprises reacting an α,β -unsaturated acid ester of formula: 60



(wherein R^1 , R^2 , R^3 and R^4 are as previously defined) with ammonium hydrosulphide, an alkali metal hydrosulphide or an alkaline earth metal hydrosulphide in the presence of carbon disulphide, and acidifying the product of the reaction. 70

The α,β -unsaturated esters of formula (II) include, for example, crotonic, isocrotonic, methacrylic, angelic, tiglic, 2-pentenoic, α -ethylacrylic, 2-hexenoic, 2-methyl-2-pentenoic, 3-methyl-2-pentenoic, α -ethylcrotonic, 2-heptenoic, 2-octenoic, 2-octadecenoic, 2,4-pentadienoic, 2,4-hexadienoic, geranic, 2,4-decadienoic, 2,4,6-octatrienoic, maleic, fumaric, citraconic, itaconic, mesaconic, glutaconic, muconic, cinnamic, hydroxycinnamic, α -phenylacrylic and methylatropic esters; and esters of crotonic, methacrylic, maleic, itaconic and cinnamic acids with alcohols having from 1 to 8 carbon atoms are preferred.

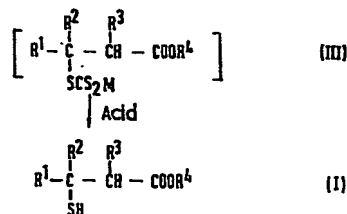
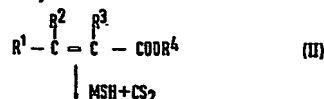
The hydrosulphide used may be, for example, potassium, sodium, calcium or ammonium hydrosulphide. Generally, the hydrosulphide is used in alcoholic solution. Examples of suitable alcohols include methanol, ethanol, isopropanol, butanol, isoamyl alcohol, ethylene glycol, propylene glycol, hexylene glycol, glycerol and cyclohexanol. Methanol, ethanol, ethylene glycol and glycerol are preferred. The alcohol may be used in admixture with another organic solvent, such as benzene, toluene or xylene. The solubility of the hydrosulphide can be improved by adding water to the alcohol; but as little water as possible should be used, if any, since the greater the amount of water, the greater the amount of thiodicarboxylic acid ester by-product produced.

The amount of hydrosulphide used should preferably be substantially equivalent to the α,β -double bond in the ester of formula (II). Although an excess of hydrosulphide can be used, this is undesirable because it results in the generation of large quantities of hydrosulphide in the subsequent acidification step. The carbon disulphide, used as the reaction medium in the process of the invention, is conveniently pre-mixed with the ester of formula (II) and then fed to the reaction system containing the hydrosulphide. However, it can also be fed in separately, at a rate determined by the amount of ester of formula (II) used. It is generally satisfactory to use an amount of carbon disulphide substantially equivalent to the α,β -double bond in the ester of formula (II), but the best yields of the desired product are obtained when using a slight excess of carbon disulphide. Thus, it is preferred to use an amount of carbon disulphide equivalent to 1.0–1.2 times the α,β -double bond in the ester of formula (II). The ester of formula (II) and/or the carbon disulphide may be mixed with another organic solvent, such as benzene, toluene, xylene, methanol or ethanol, if desired.

The reaction between the ester of formula (II), the hydrosulphide and the carbon disulphide is normally carried out as a batch process, by gradually adding the ester, or the mixture of ester and carbon disulphide, to

the solution of the hydrosulphide; but it may also be performed as a continuous process, by continuously feeding the ester (II), hydrosulphide and carbon disulphide into a reaction system, at appropriate rates. The reaction temperature and pressure are not critical, but the reaction is preferably performed at a temperature below 80°C. The reaction is exothermic and is quickly completed.

Although the reaction mechanism has not yet been fully elucidated, it is believed that the reaction proceeds as shown in the following scheme (wherein R^1 , R^2 , R^3 and R^4 are as previously defined, and M represents an ammonium group or an alkali or alkaline earth metal).



It is believed that, in the first step of the process of the invention, the carbon disulphide reacts with the hydrosulphide MSH, to form a salt of a halogenated thiocarbonic acid. Addition of the salt to the α,β -double bond of the ester (II) quickly gives the intermediate of formula (III). This intermediate decomposes when acidified, giving the desired mercaptocarboxylic acid ester of formula (I), with regeneration of the carbon disulphide. The acid used for this acidification step may be, for example, hydrochloric or sulphuric acid.

The desired product can be isolated and purified by conventional techniques. For example, if it is readily soluble in water, it is extracted into an organic solvent such as benzene, and the extract is fractionated. On the other hand, if the desired product is relatively insoluble in water, it can be separated and fractionated without addition of an organic solvent. The crude mercaptocarboxylic acid ester thus isolated can be purified by distillation or recrystallization, to remove by-products such as thiodicarboxylic acid esters.

The invention is illustrated by the following Examples. The following analytical instruments were used to obtain the results recorded in the Examples: gas chromatograph Model 4B-PT, manufactured by Shimadzu Manufacturing Co.; infrared spectrophotometer Model EPJ-G3, manufactured by Hitachi Manufacturing Co.; and nuclear magnetic resonance spectrometers models T-60 (60 MHz, 14,092

Gauss), and XL-100FT (100 MHz, 23,490 Gauss), manufactured by Varian Co.

Example 1

5 Methyl 2 - methyl - 3 - mercaptopropionate
A mixture of 100.1 g of methyl methacrylate and 93.2 g of carbon disulphide was added with stirring, over a period of about 45 minutes, to a solution of 80.0 g of sodium hydrosulphide (containing 70.56% of pure sodium hydrosulphide and 2.34% of sodium sulphide) in 100 g of methanol. The reaction mixture turned orange and then dark red, while an exothermic reaction quickly took place. The reaction temperature was maintained at 30—40°C.

10 The reaction mixture was then acidified to pH 1 by gradually adding 120 g of concentrated hydrochloric acid. Its colour turned from dark red to yellow, with evolution of hydrogen sulphide, precipitation of sodium chloride, and regeneration of carbon disulphide. About 160 ml of water were added and the resulting mixture was stirred, to dissolve the precipitated sodium chloride. On being allowed to stand, the mixture divided into an aqueous layer and an oily layer. The yellow oily layer was separated from the aqueous layer and the carbon disulphide was distilled off from it. The residue was distilled under reduced pressure, giving 79.8 g of a transparent colourless fraction at 52—54°C/8 Torr, refractive index (25°C) 1.4569 (yield: 59.5%).

20 It was confirmed by gas chromatography that the product was a single compound, free from impurities. The results of IR and NMR spectroscopy were as follows:—

IR:

1170, 1740 and 2580 cm⁻¹
(No absorptions were observed at 1655 and 3050 cm⁻¹)

NMR:

1.0—1.4 (CH₃—, d, 3H)
1.2—1.6 (HS—, t, 1H)
2.3—3.0 (—CH₂—CH<, m, 3H)
3.6—3.8 (H₃COOC—, s, 3H).

(internal standard TMS; 10% carbon tetrachloride solution; sample concentration 30%).

50 These results confirm the disappearance of the double bond in the starting material, the presence of the ester group, and the formation of the 3 - mercapto - derivative. Iodometry of the product gave the result SH: 24.47% (theoretical value: 24.64%). It was thus confirmed that the product was methyl 2 - methyl - 3 - mercaptopropionate.

Example 2

2-Ethylhexyl 2 - methyl - 3 - mercaptopropionate
60 A mixture of 203.0 g of 2-ethylhexyl meth-

acrylate and 95.4 g of carbon disulphide was added with stirring, over a period of about 2 hours, to a solution of 83.0 g of sodium hydrosulphide (containing 70.56% of pure sodium hydrosulphide) in 124 g of methanol, and the resulting mixture was kept stirred for a further 2½ hours. The reaction mixture was maintained at a temperature of 45—55°C.

The reaction mixture was then treated in the same way as in Example 1, to give a yellow oily residue. This residue was distilled under reduced pressure, giving 141.9 g of a colourless transparent fraction at 96°C/3.5 Torr, refractive index (25°C) 1.4562 (yield: 59.7%).

It was confirmed by gas chromatography that the product was a single compound, free from impurities. The results of IR spectroscopy were as follows:—

IR:

1170, 1740 and 2580 cm⁻¹
(No absorptions were observed at 1655 and 3050 cm⁻¹).

Iodometry of the product gave the result SH: 14.09% (theoretical value: 14.23%). It was thus confirmed that the product was 2-ethylhexyl 2 - methyl - 3 - mercaptopropionate.

Example 3

Methyl 3 - methoxycarbonyl - 3 - mercaptopropionate

A mixture of 144.1 g of dimethyl maleate and 93.2 g of carbon disulphide was added with stirring, over a period of about 85 minutes, to a solution of 80.0 g of sodium hydrosulphide (containing 70.56% of pure sodium hydrosulphide) in 100 g of methanol. The reaction mixture was maintained at a temperature of 0—10°C.

The reaction mixture was then treated in the same way as in Example 1 to give a yellow oily residue, and distillation of the residue obtained gave 119.7 g of a colourless transparent fraction at 104°C/9 Torr, refractive index (25°C) 1.4662 (yield: 67.2%).

It was confirmed by gas chromatography that the product was a single compound, free from impurities. The results of IR spectroscopy were as follows:—

IR:

1170, 1740 and 2580 cm⁻¹
(No absorptions were observed at 1655 and 3050 cm⁻¹).

Iodometry of the product gave the result SH: 18.39% (theoretical value: 18.56%). It was thus confirmed that the product was methyl 3 - methoxycarbonyl - 3 - mercaptopropionate.

Example 4

Methyl 3-mercaptopropionate

A mixture of 103.2 g of methyl crotonate and 93.2 g of carbon disulphide was added with stirring, over a period of about 60 minutes, to a solution of 80.0 g of sodium hydrosulphide (containing 70.56% of pure sodium hydrosulphide) in 100 g of methanol. The reaction mixture was maintained at a temperature of 0–10°C.

The reaction mixture was then treated in the same way as in Example 1, to give a yellow oily residue. This residue was distilled under reduced pressure, giving 100.8 g of a colourless transparent fraction at 59°C/19 Torr, refractive index (25°C) 1.4532 (yield: 75.2%).

It was confirmed by gas chromatography that the product was a single compound, free from impurities. The results of IR and NMR spectroscopy were as follows:—

IR:

1170, 1740 and 2580 cm^{-1}
(No absorptions were observed at 1655 and 3050 cm^{-1})

NMR:

1.3–1.5 (CH_3 —, d, 3H)
1.6–1.9 (HS —, d, 1H)
2.4–2.7 ($-\text{CH}_2$ —, d, 2H)
2.8–3.6 ($-\text{CH}$ —, m, 1H)
3.6–3.8 ($-\text{COOCH}_3$ —, s, 3H).

These results confirmed the disappearance of the double bond in the starting material, the presence of the ester group, and the formation of the 3-mercapto-derivative. Iodometry of the product gave the result SH: 24.44% (theoretical value: 24.64%). It was thus confirmed that the product was methyl 3-mercaptopropionate.

Example 5

Methyl 2-methoxycarbonylmethyl-3-mercaptopropionate

A mixture of 158.0 g of dimethyl itaconate, 93.2 g of carbon disulphide and 90 g of methanol was added with stirring, over a period of about 60 minutes, to a solution of 80.0 g of sodium hydrosulphide (containing 70.56% of pure sodium hydrosulphide) in 100 g of methanol. The reaction mixture was maintained at a temperature of 20–30°C.

The reaction mixture was then treated in the same way as in Example 1, to give a yellow oily residue. This residue was distilled under reduced pressure, giving 159.9 g of a transparent colourless fraction at 109–110°C/3.5 Torr, refractive index (25°C) 1.4710 (yield: 83.3%).

It was confirmed by gas chromatography that this product was a single compound, free from impurities. The results of IR and NMR spectroscopy were as follows:—

IR:

1170, 1740 and 2580 cm^{-1}
(No absorptions were observed at 1655 and 3050 cm^{-1}).

NMR:

1.3–1.7 (HS —, t, 1H)
2.4–3.2 ($-\text{CH}_2-\text{CH}-\text{CH}_2$ —, m, 5H)
3.5–3.8 [$-(\text{COOCH}_3)_2$ —, d, 6H].

These results confirm that the double bond of the starting material had disappeared in the product, that the ester group was present, and that the 3-mercapto-derivative had been formed. Iodometry of the product gave the result SH: 17.27% (theoretical value 17.20%). It was thus confirmed that the product was methyl 2-methoxycarbonylmethyl-3-mercaptopropionate.

Example 6

Methyl 3-mercapto-3-phenylpropionate

A mixture of 162.2 g of methyl cinnamate, 93.2 g of carbon disulphide and 90 g of methanol was added with stirring, over a period of about 60 minutes, to a solution of 80.0 g of sodium hydrosulphide (containing 70.56% of pure sodium hydrosulphide) in 100 g of methanol. The reaction mixture was maintained at a temperature of 35–45°C.

The reaction mixture was then treated in the same way as in Example 1, to give a yellow oily residue. This residue was distilled under reduced pressure, giving 132.2 g of a transparent colourless fraction at 109–111°C/4.5 Torr, refractive index (25°C) 1.5447 (yield: 67.4%).

It was confirmed by gas chromatography that this product was a single compound, free from impurities. The results of IR and NMR spectroscopy were as follows:—

IR:

1170, 1740 and 2580 cm^{-1}
(No absorptions were observed at 1655 and 3050 cm^{-1})

NMR:

2.0–2.3 (HS —, d, 1H)
2.7–3.0 ($-\text{CH}_2$ —, d, 2H)
3.5–3.7 (H_3COOC —, s, 3H)
4.2–4.6 ($-\text{CH}$ —, q, 1H)
7.0–7.6 (C_6H_5 —, m, 5H).

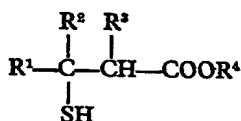
[The value for $-\text{CH}_2$ — shifted 0.10 ppm higher than that for $-\text{CH}$ — when using EU(fod)₃].

These results confirm that the double bond of the starting material had disappeared in the product, that the ester group was present, and that the 3-mercapto-derivative had been formed. Iodometry of the product gave the result SH: 16.65% (theoretical value: 16.85%). It was thus confirmed that

the product was methyl 3 - mercapto - 3 - phenylpropionate.

WHAT WE CLAIM IS:—

1. A process for preparing a mercaptocarboxylic acid ester of formula:

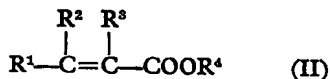


(I)

wherein:

- each of R^1 , R^2 and R^3 is a hydrogen atom, an alkyl group, an unsaturated hydrocarbon group, a carboxy-substituted alkyl group, a carboxy-substituted unsaturated hydrocarbon group, an alkoxy-carbonyl-substituted alkyl group, an alkoxy-carbonyl-substituted unsaturated hydrocarbon group, a phenyl group, a substituted phenyl group, a carboxyl group or an alkoxy-carbonyl group, provided that R^1 , R^2 and R^3 may not all simultaneously be hydrogen atoms; and

- R^4 is a phenyl or substituted phenyl group, or a residue derived by removal of a hydroxyl group from an alcohol; which comprises reacting an α, β -unsaturated acid ester of formula:



- (wherein R^1 , R^2 , R^3 and R^4 are as previously defined) with ammonium hydrosulphide, an alkali metal hydrosulphide or an alkaline earth metal hydrosulphide in the presence of carbon disulphide, and acidifying the product of the reaction.

2. A process according to claim 1, in which the amount of carbon disulphide used is 1.0—1.2 times equivalent to the α, β -double bond in said ester of formula (II).

3. A process according to claim 1 or claim 2, in which said ester of formula (II) is an ester of crotonic, methacrylic, maleic, itaconic or cinnamic acid with an alcohol having from 1 to 8 carbon atoms.

4. A process according to any preceding claim, in which said hydrosulphide is potassium hydrosulphide, sodium hydrosulphide or calcium hydrosulphide.

5. A process according to any preceding claim, in which said hydrosulphide is used in an alcoholic solution.

6. A process according to claim 5, in which the hydrosulphide is used in solution in methanol, ethanol, ethylene glycol or glycerol.

7. A process according to any preceding claim, in which the reaction is carried out at a temperature below 80°C .

8. A process according to any preceding claim, in which the product of the reaction is acidified with sulphuric or hydrochloric acid.

9. A process according to claim 1, substantially as herein described in any of the Examples.

10. Mercaptocarboxylic acid esters of formula (I), as set forth in claim 1, when prepared by a process according to any preceding claim.

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